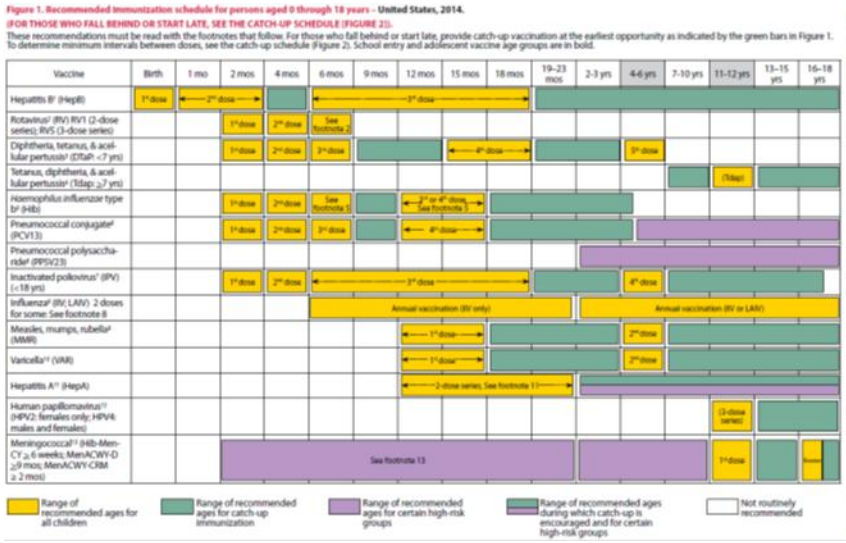
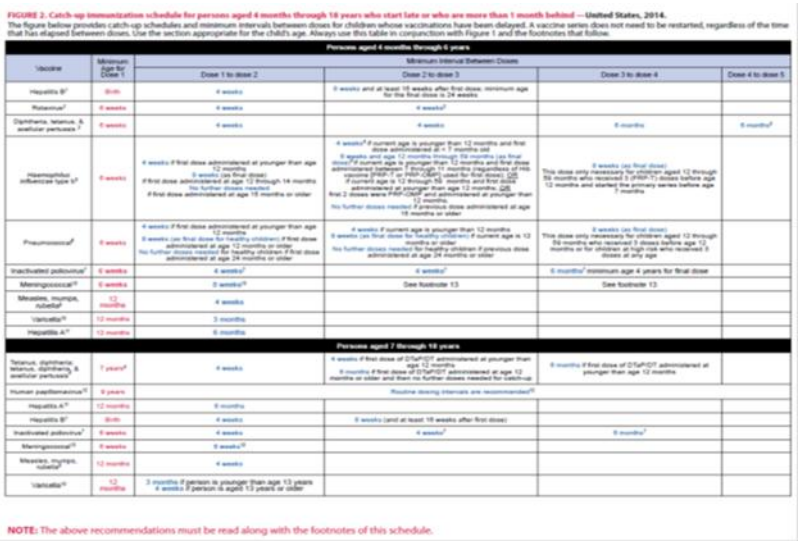
Taking ACIP Footnotes in Stride

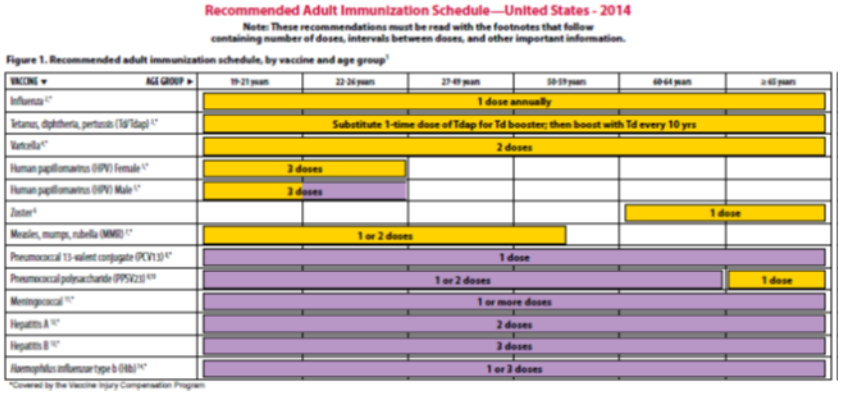
Karen Lewis, M.D.

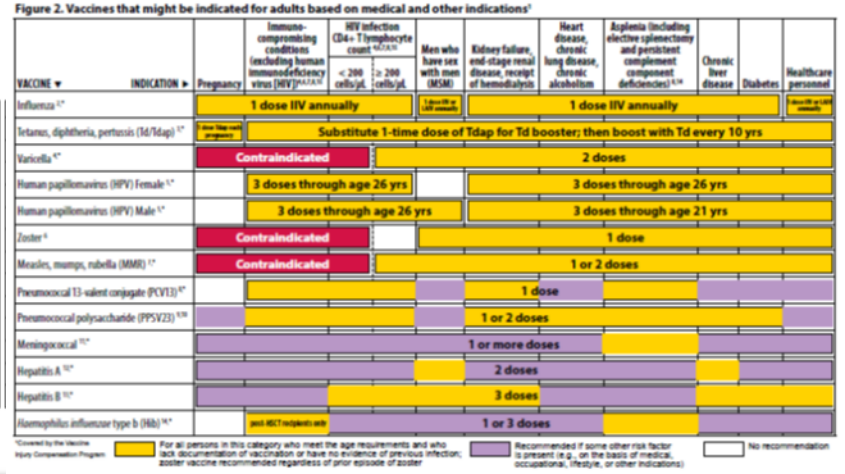
April 23 & 24, 2014

CDC Pediatric and Adult Schedules 2014



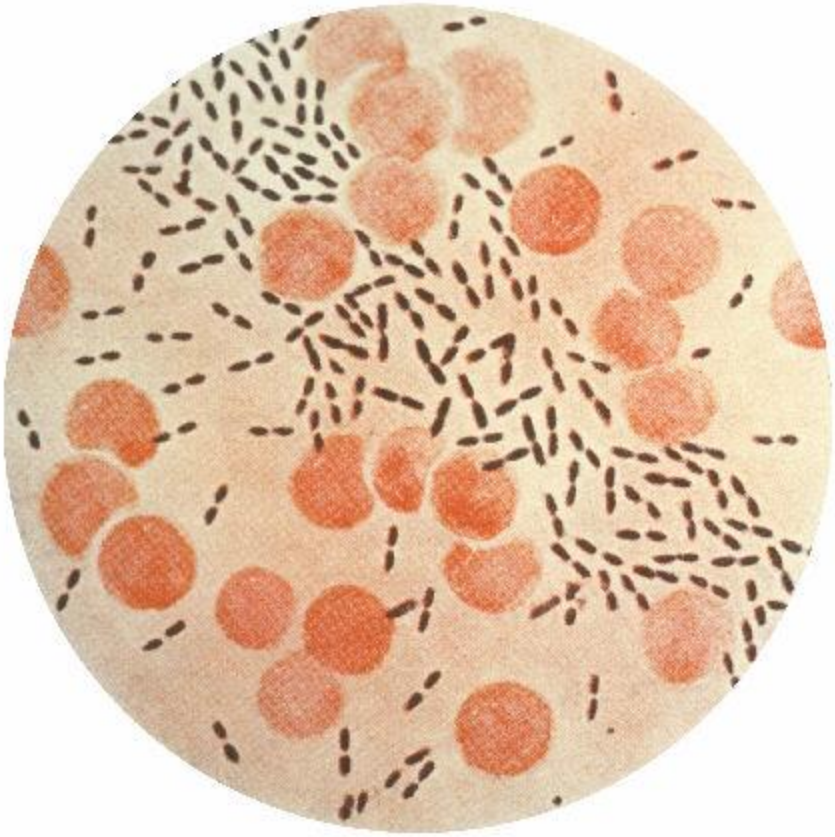


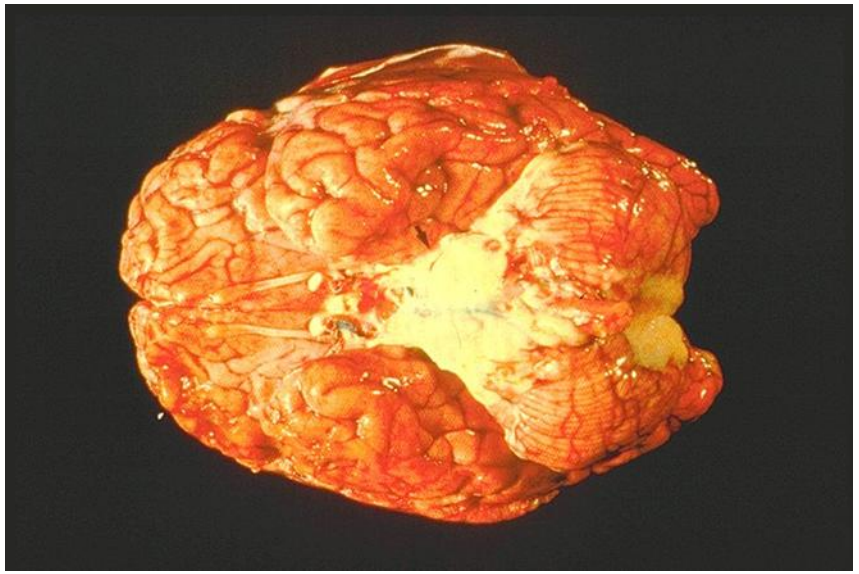




http://www.cdc.gov/vaccines/schedules/index.html

Streptococcus pneumoniae





History of Pneumococcal Vaccines

- 1977: 14-valent polysaccharide vaccine
- 1983: 23-valent polysaccharide vaccine (PPSV23)
- 2000: 7-valent polysaccharide conjugate vaccine (PCV7)
- 2010: 13-valent polysaccharide conjugate vaccine (PCV13)

Groups at High Risk for *Streptococcus pneumoniae*

- Elderly
- Infants/young children
- Asplenia
- Sickle cell disease & hemoglobinopathies
- Native American/AN
- African American
- Child care attendance
- Long term care facility resident
- CSF leak
- Cochlear implant
- Immunocompromise
  - HIV
  - Congenital
  - Malignancy
  - Chemotherapy
  - Radiation therapy
  - Immunosuppressive drugs
  - Transplantation
- Chronic heart, lung, liver, renal disease
- Diabetes
- Smoking
- Alcoholism

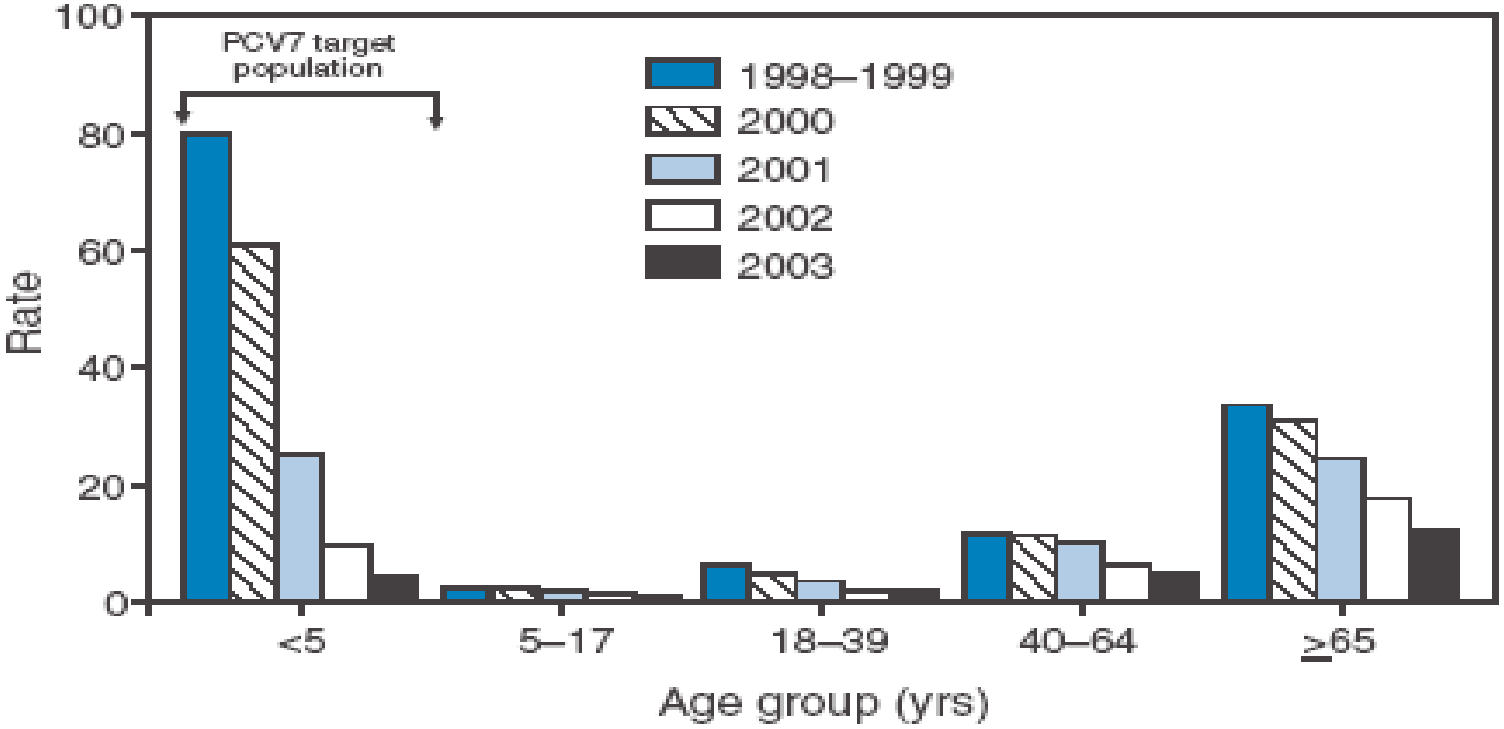
PPSV23 Vaccine in Adults

- One dose ≥ 65 years old
- Use in High Risk younger adults
- One time PPSV23 revaccination after 5 years
  - HIV
  - Immunocompromised
  - Chronic renal failure
  - Nephrotic syndrome
  - Sickle cell anemia and other hemoglobinopathies
  - Asplenia
- PPSV23 when ≥ 65 years and ≥ 5 years since last PPSV23

Pneumococcal Vaccine Principles

- Polysaccharide vaccine poorly effective in children less than 2 years old
- Conjugate vaccine is more immunogenic for all
  - Effective in infancy
- High risk individuals benefit from both conjugate and polysaccharide vaccines
- More immunogenic if give conjugate before polysaccharide

FIGURE 1. Rate* of vaccine-type (VT) invasive pneumococcal disease (IPD) before and after introduction of pneumococcal conjugate vaccine (PCV7), by age group and year — Active Bacterial Core surveillance, United States, 1998–2003



* Per 100,000 population.

† For each age group, the decrease in VT IPD rate for 2003 compared with the 1998–1999 baseline is statistically significant ($p<0.05$).

MMWR Sept. 16, 2005

Invasive *S. pneumoniae* in Arizona Children ≤ 5 y.o. 2008 (N=133)

Vaccine	Vaccine Serotypes	Cases
Prevnar 7 (PCV7)	6B	1
	4, 9V,14,18C,19F, 23F	0

Invasive *S. pneumoniae* ≤ 5 y.o. in AZ, 2008 (N=133)

Vaccine	Vaccine Serotypes	Cases
Prevnar 7 (PCV7)	6B	1
	4, 9V,14,18C,19F, 23F	0
Prevnar 13 (PCV7 + six)	1	3
	3	1
	5	12
	6A	1
	7F	16
	19A	13

Invasive *S. pneumoniae* ≤ 5 y.o. in AZ, 2008 (N=133)		
Vaccine	Vaccine Serotypes	Cases
Prevnar 7 (PCV7)	6B	1
	4, 9V,14,18C,19F, 23F	0
Prevnar 13 (PCV7 + six)	1	3
	3	1
	5	12
	6A	1
	7F	16
	19A	13
Pneumovax 23 (PCV13 without 6A + eleven)	8	1
	12F	1
	15B	2
	2, 9N, 10A, 11A, 17F, 20, 22F, 33F	0

Schedule for PCV13 Vaccines

- Minimum age
  - 6 weeks
- Four doses
  - 2, 4, 6 months and 12-15 months
- Fewer total PCV13 doses if the start of PCV13 dosing is delayed

Pneumococcal Conjugate Vaccine (PCV-13) Schedule for Older Unimmunized Children

Age at 1st Dose	Primary Series	Booster
7-11 months	2 doses	Yes*
12-23 months	2 doses*	No
24-59 months, healthy	1 dose	No
24-71 months, medical conditions	2 doses*	No

*separated by at least 8 weeks

MMWR. 2010: 59 (RR-11), 1-19

Broadening High Risk Pediatric Pneumococcal Coverage

- High risk children need both PCV-13 and PPSV-23
  - HIV and other immunocompromising conditions
  - Functional or anatomic asplenia, including sickle cell disease
  - Cochlear implant or CSF leak
- After PCV-13 in infancy, give PPSV23 at ≥ 2 years old
  - Then 2nd PPSV23 in ≥ 5 years for
    - HIV and other immunocompromising conditions
    - Functional or anatomic asplenia, including sickle cell disease
    - No more PPSV23 until 65 years old
- Unimmunized high risk 6 -18 years:
  - One dose PCV-13 and in ≥ 8 weeks, give PPSV-23

MMWR June 28, 2013

PCV13 for High-Risk Adults 19-64 yo

- If not previously received PCV13 or PPSV23
  - PCV13 followed in ≥ 8 weeks by PPSV23
  - If previous PPSV23, follow in 1 year by PCV13
- High Risk adults
  - Immune compromised* and HIV*
  - Chronic renal failure* and nephrotic syndrome*
  - Asplenia* & sickle cell disease*
  - CSF leak or cochlear implants

*Repeat PPSV23 in 5 years

MMWR. October 12, 2012

Prospective Pneumococcal Protection

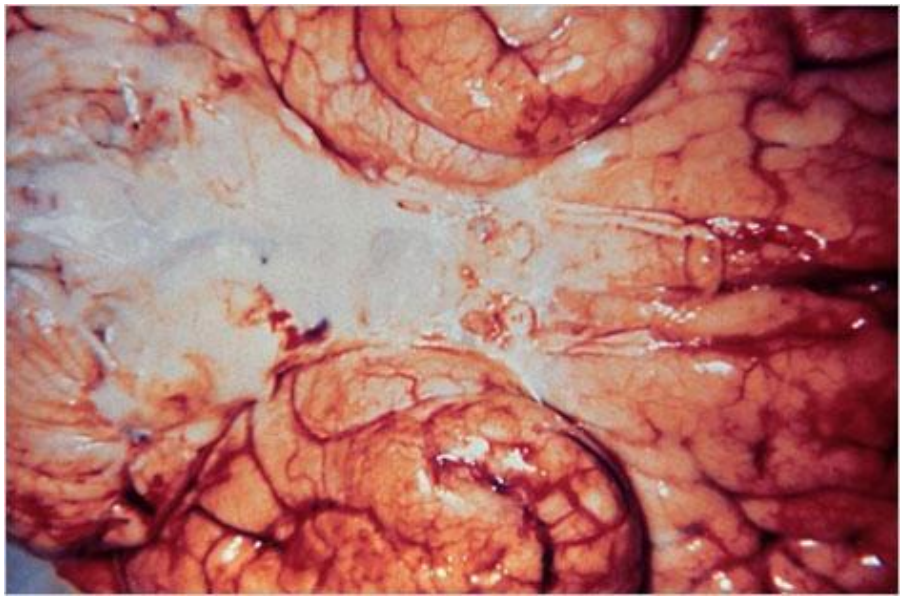
- Give pneumococcal vaccine(s), Hib, and MCV4 before:
  - Elective splenectomy
  - Cochlear implant
  - Immunosuppressive therapy
- Best to give at least 2 weeks for antibody response
- Optimally PCV13 before PPSV23

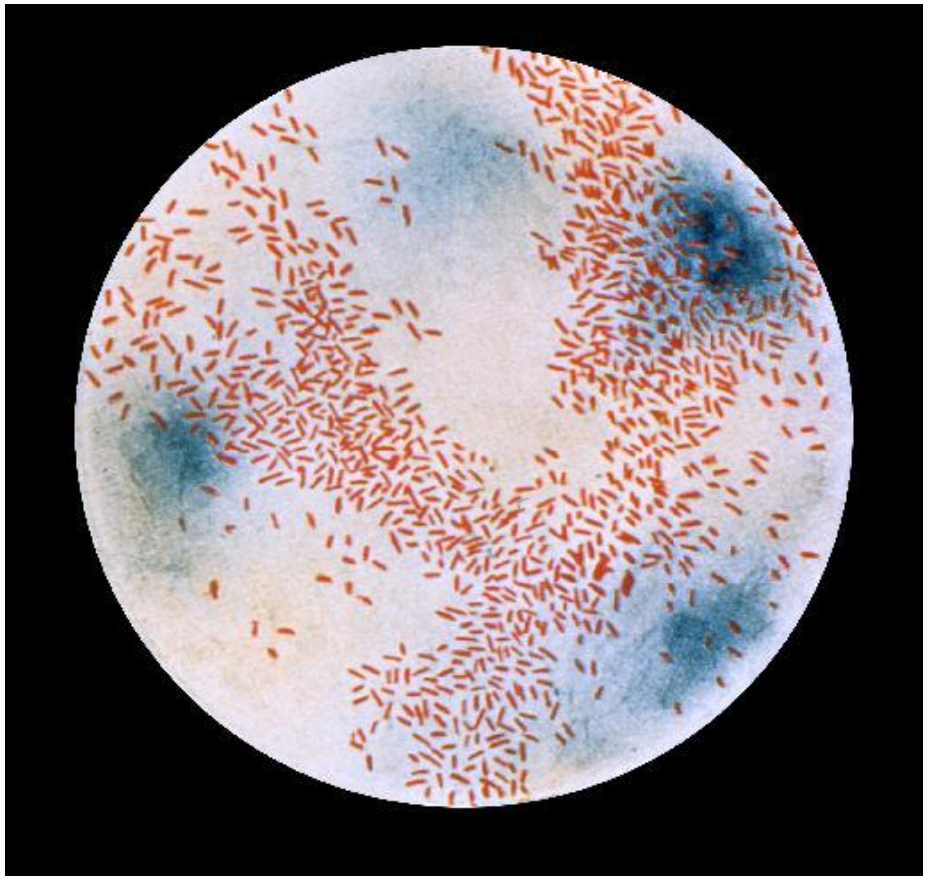
Summary of High Risk Patients

- PCV13 infancy or ASAP
- PPSV23 when ≥ 2 years old
- Need both PCV13 and PPSV23
- PCV13 before PPSV23 when possible

- Repeat PPSV23 once in 5 years
  - HIV
  - Immune suppression
  - Chronic renal failure
  - Nephrotic syndrome
  - Sickle cell disease, etc.
  - Asplenia
- Final PPSV23 at ≥ 65 years old

Haemophilus influenzae type b (Hib)





US & Hib	Early 1980s	2007
Cases	~20,000	202
Meningitis	~10,000	N/A

Risk Factors for Invasive Hib Disease

- Infants
- Children under 5 years old
- American Indian/Alaska Native
- Sickle cell disease
- Functional or anatomic asplenia
- HIV infection
- Chemotherapy or radiation therapy for malignancy
- Immunoglobulin deficiency including IgG2 subclass deficiency
- Early component complement deficiency
- Receipt of hematopoietic stem cell transplant

MMWR. February 28, 2014

Invasive Hib in < 5 y.o. Children

Rate per 100,000

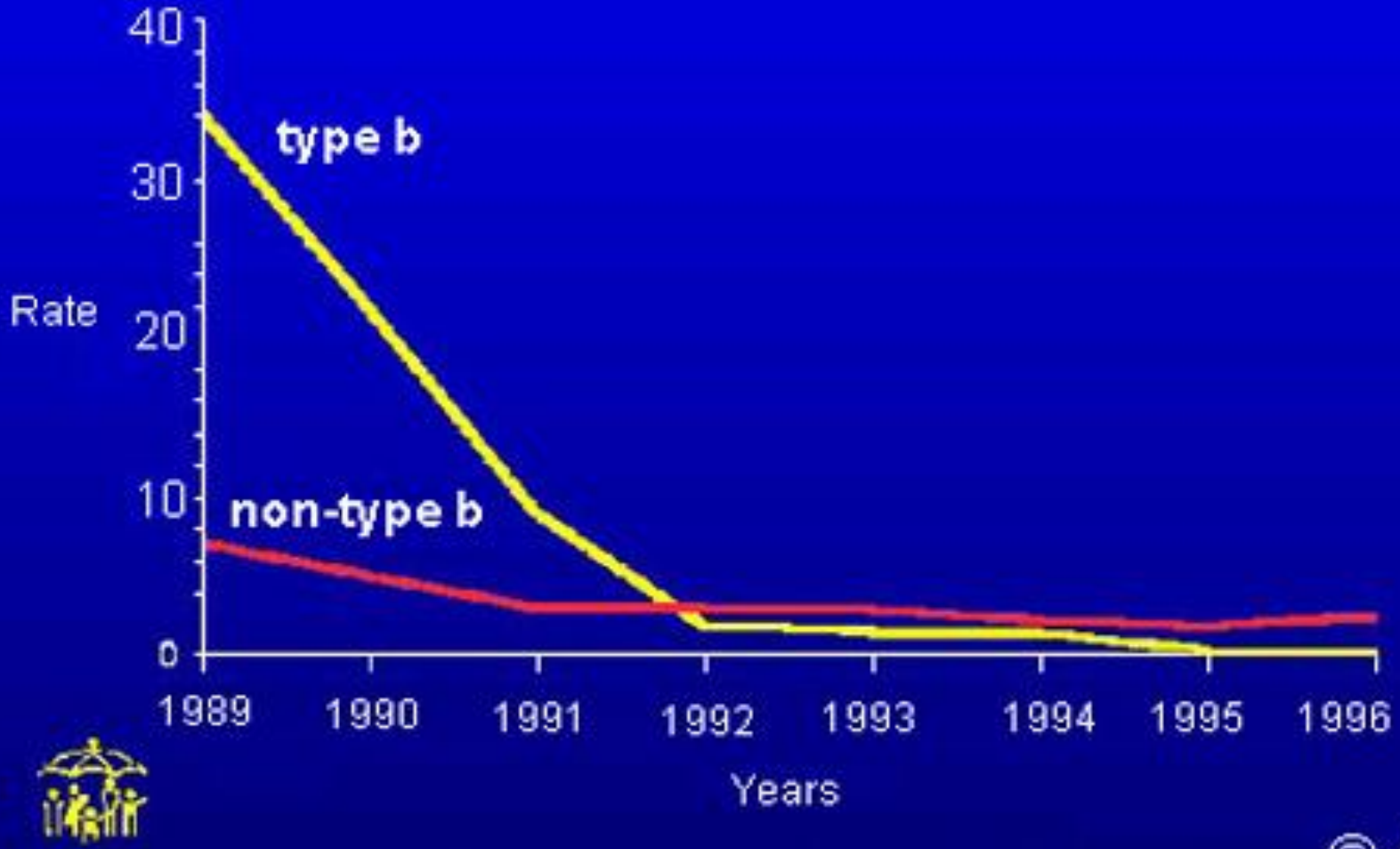
	Before Vaccination	After Vaccination	Postvaccine Rate Year
United States	60-100	0.3	1996
Alaskan Native	601	5.4	2001-2004
White Mountain Apache	250	22	1992-1999
Navajo	152	22	1992-1999

Singleton Arch Pediatr Adolesc Med May 2009

Development of Hib Vaccines

- Hib polysaccharide vaccine 1985-1988
  - 18 months-4 years old
- Hib conjugate vaccine 1987
  - Effective in infancy
  - Type of conjugation
    - Hib—Neisseria outer membrane protein
      - 2 doses infancy & booster
      - More effective in Native American
    - Hib—tetanus: 3 doses infancy & booster

Haemophilus influenzae type b (Hib) and non-type Invasive Disease, per 100,000 Population, United States, 1989-1996*



*For children aged <6 years; calculated from four active laboratory-based surveillance areas.

Different Hib Vaccines

- 6 weeks – 4 years
  - PRP-OMP:
    - PedvaxHIB
    - COMVAX (Hib-HepB)
  - PRP-T:
    - Pentacel (DTap-IPV/Hib)
    - MenHibrix (MenCY-Hib)
- 15 months – 4 years (package insert)
  - Hiberix (PRP-T)
    - Final dose during 12 mo-4 years for child who had at least one previous Hib dose

Vaccination Schedule for Hib

Vaccine	Age at 1st Dose	Primary Series	Booster
PRP-T	2-6 mos	3 doses, 8 wks apart	12-15 mos*
	7-11 mos	2 doses, 8 wks apart	12-15 mos*
	12-14 mos	1 dose	8 weeks later
	15-59 mos	1 dose	---
PRP-OMP	2-6 mos	2 doses, 8 wks apart	12-15 mos*
	7-11 mos	2 doses, 8 wks apart	12-15 mos*
	12-14 mos	1 dose	8 weeks later
	15-59 mos	1 dose	---

CDC Pink Book, 12th edition and CDC Schedule 2014

*≥ 8 weeks after previous dose

5-18 Year Olds who Need One Dose of Hib Vaccine

- Not fully immunized against Hib
  - Definition
    - Lacking primary series & booster, or
    - Lacking booster ≥ 15 months
- Give to children ages 5-18 years old
  - HIV-infected
  - Anatomic or functional asplenia, including sickle cell disease

MMWR. Feb. 28, 2014

Neisseria meningitidis

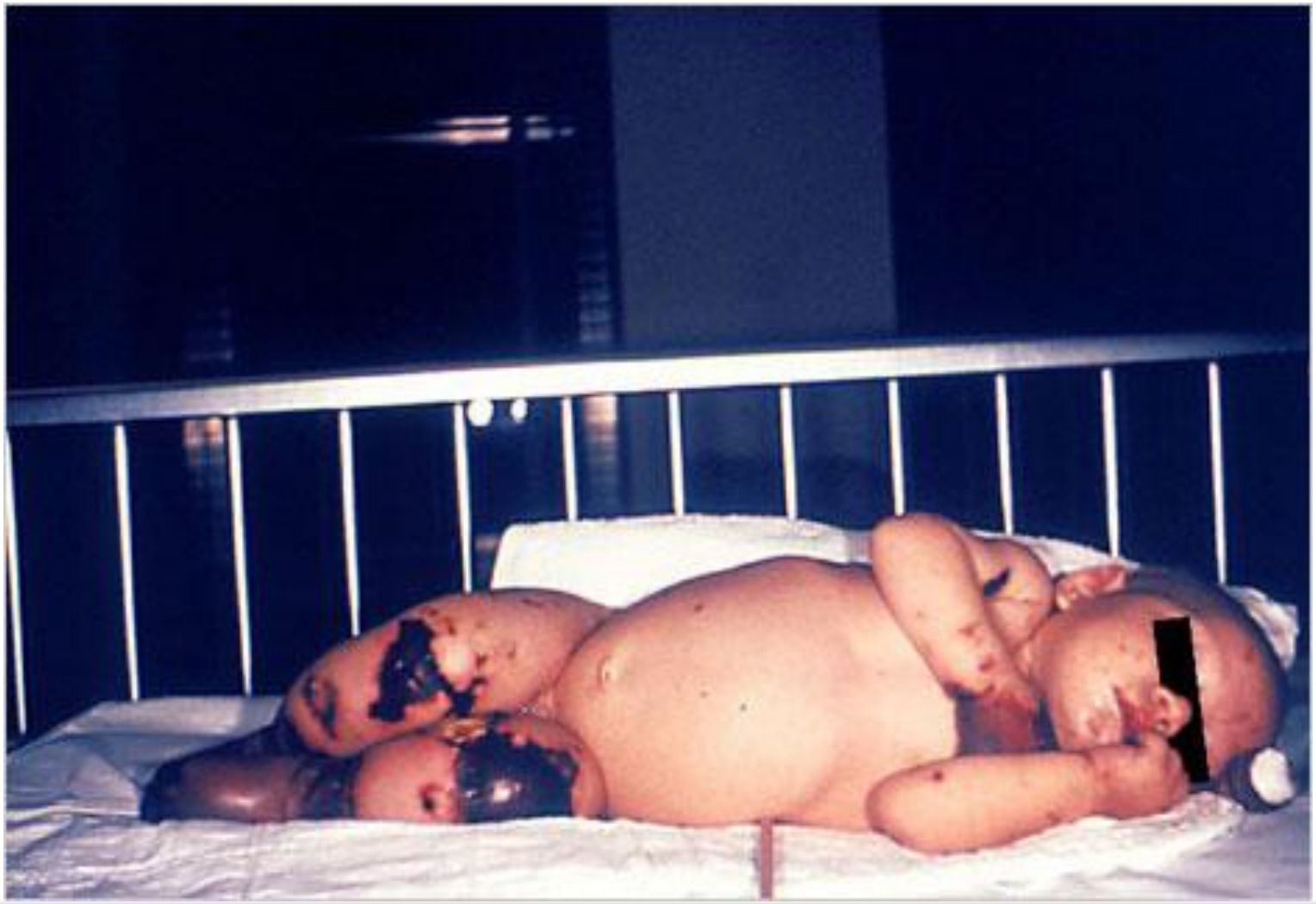
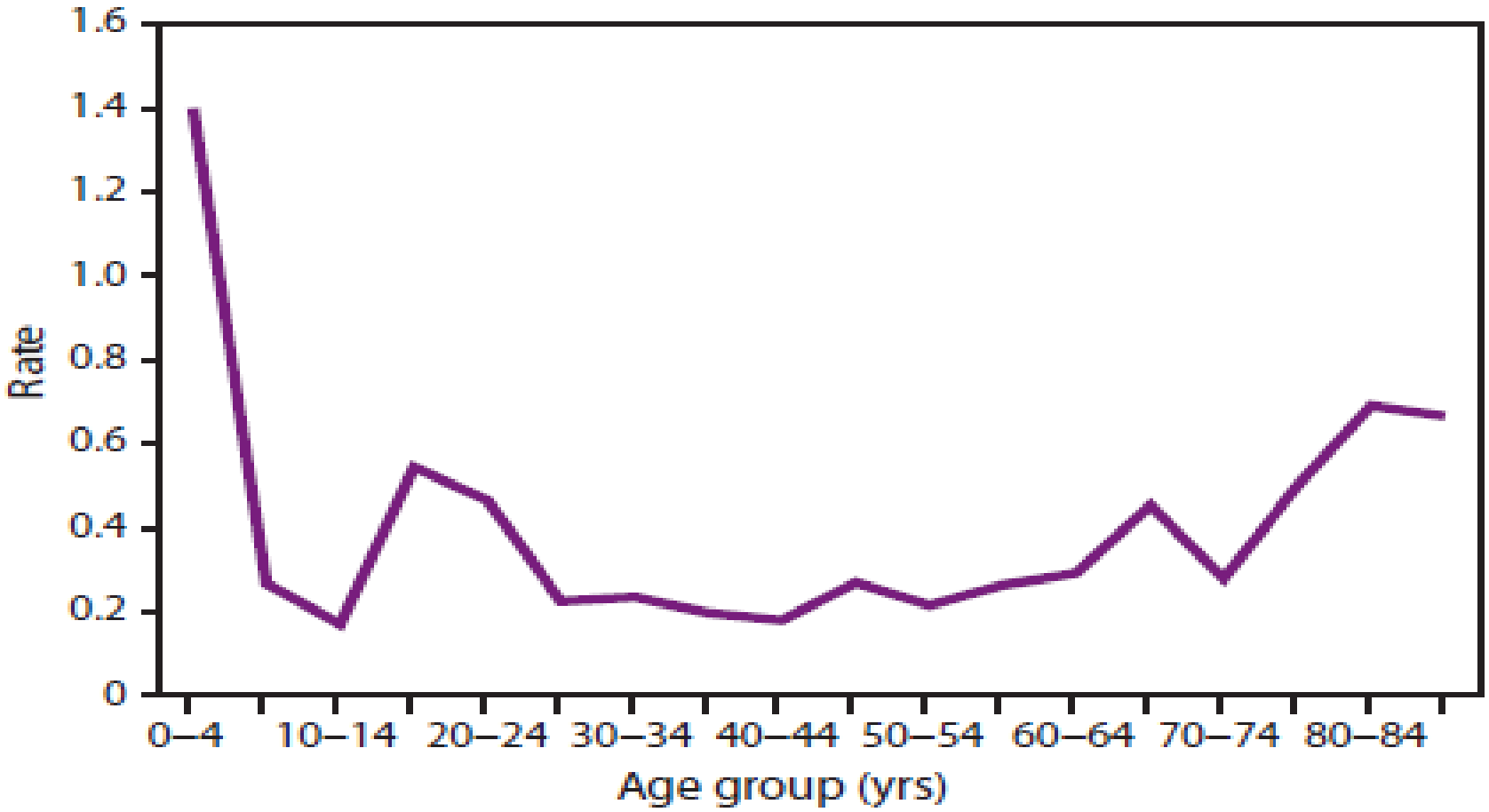


FIGURE 2. Rate* of meningococcal disease, by age group — United States, 2002–2011†



MMWR. March 22, 2013

High Risk for Meningococcal Disease

- Infants
- Adolescents
- Asplenia, including sickle cell disease
- Complement component deficiency
- Travel to meningococcal endemic area
- Microbiologists working with *N. meningitidis*
- Military recruits
- Local outbreaks

Meningococcal Vaccines

- Quadrivalent (serogroups A, C, Y, W135)
  - Polysaccharide
    - Menomune ≥ 2 yrs old
  - Conjugated
    - Menactra (MCV4) 9 mos-55 yrs
    - Menveo (MCV4) 2 mos-55 yrs
    - MenHibrix (Hib-MenCY) 6 wks-18 mos

Routine Adolescent Meningococcal Vaccine

Primary	Booster
11-12 yo	16 yo
13-15 yo	16-18 yo
≥ 16 yo	---

HIV-infected adolescents need
a 2-dose primary series, ≥ 2 months apart

Menveo for High Risk Patients

- Four doses
  - 2, 4, 6 months with booster at 12 months
- Two doses
  - If start 7-23 months
    - 2nd dose after 12 months and ≥ 3 months after 1st
  - Start ≥ 2 years old
    - Two doses, ≥ 2 months apart
- One dose
  - Traveler to endemic area ≥ 2 years old to 55 years

Menactra for High Risk Patients

- Do not give Menactra to child with asplenia or sickle cell disease until ≥ 2 years old and at least 4 weeks after last pneumococcal vaccine
- 9-23 months: Two doses, ≥ 3 months apart
- ≥ 2 years old: Two doses, ≥ 2 months apart
- Traveler to endemic area:
  - 9-23 months: Two doses
  - ≥ 2 years old to 55 years old—One dose

MenHiberix (Hib-MenCY) for High Risk Patients

- 2, 4, 6 months with booster 12-15 months
- Fourth dose can be given as late as 18 months

- If 1st dose given ≥ 12 months, 2 doses ≥ 8 weeks apart

➢ Does not fulfill requirement for travel to African meningitis belt or pilgrimage to the Hajj

Menommune

- Polysaccharide licensed in 1978
- Serogroups A, C, Y, W135
- Licensed ≥ 2 years old
- MCV4 preferred when multiple doses needed and MCV4 previously received
- Use Menommune ≥ 56 years old
  - Single dose for travel
  - Other one-time need

Repeating Meningococcal Vaccine

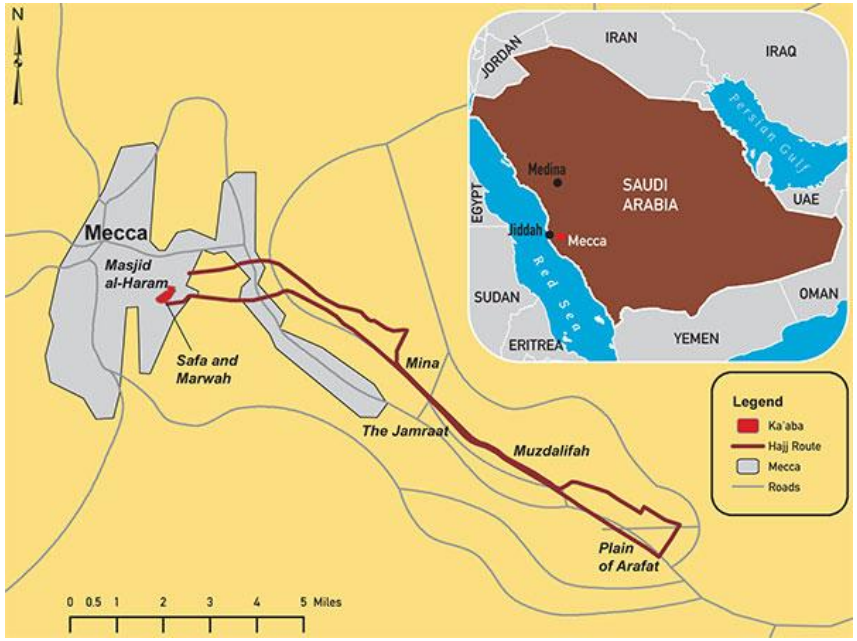
<u>If risk persists</u>:

- 1st dose(s) **2 mo – 6 yo**
- F/U vaccine in **3** yrs→ then every **5** yrs

- 1st dose(s) ≥ **7 yo**
- F/U vaccine in **5** yrs→ then every **5** years

Countries at Higher Risk for Meningococcal Disease

Meningitis Belt
CDC Yellow Book 2012



Hajj Pilgrimage
Oct. 2-7, 2014

Meningococcal Vaccines & Hajj

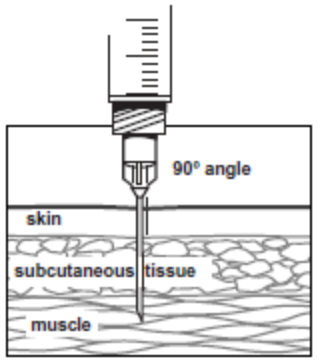
- Proof of vaccine needed for visa
- Vaccine required within 3 years & not less than 10 days
- Children ≥ 2 yo and adults
  - Quadrivalent A/C/Y/W-135
- Infants 3 mo-23 months
  - Monovalent A
    - » 2 doses, with a 3 month interval between doses

http://www.hajinformation.com/main/p3001.htm

Types of Influenza Vaccines

Inactivated

IM



Intradermal

Live Attenuated

Intranasal

Egg-Based Influenza Vaccine Process

World Health Organization

CDC
Centers for Disease Control and Prevention

FDA U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Licensed Influenza Vaccines for Children and Adults as of April 2014

Manufacturer	Trade Name	Ages	Abbreviation
Newly licensed			
Medimmune	FluMist Quadrivalent	2-49 ys healthy	LAIV4
GSK	Fluarix Quadrivalent	≥ 3 years	IIV4
Sanofi Pasteur	Fluzone Quadrivalent	≥ 6 months	IIV4
Previously licensed			
Medimmune	FluMist	2-49 yrs healthy	LAIV3
CSL	Afluria	≥ 9 years	IIV3
GSK	Fluarix	≥ 3 years	IIV3
Novartis	Fluvirin	≥ 4 years	IIV3
Sanofi Pasteur	Fluzone	≥ 6 months	IIV3

Influenza Vaccines for Adults as of April 2014

Manufacturer	Trade Name	Ages	Abbreviation
Newly Licensed			
Novartis	Flucelvax	≥ 18 yrs	ccIIV3
Protein Sciences	FluBlok	18-49 yrs	RIV3
Previously Licensed			
GSK	FluLaval	≥ 18 yrs	IIV3
Novartis	Agriflu	≥ 18 yrs	IIV3
Sanofi Pasteur	Fluzone Intradermal	18-64 yrs	IIV3
Sanofi Pasteur	Fluzone High Dose	≥ 65 yrs	IIV3

FLUCELVAX (ccIIV3)

- Viruses need to grow in cells
- Influenza viruses grown in dog kidney cells
- Liquid nutrients keep cells alive
- Harvest influenza virus and create trivalent vaccine

FLUBLOK (RIV3)
Made by Recombinant Technology

- Genetic material for influenza hemagglutinin inserted into a moth virus' genetic material
- Moth virus added to continuously growing cells from fall armyworm
- Influenza hemagglutinin produced and harvested

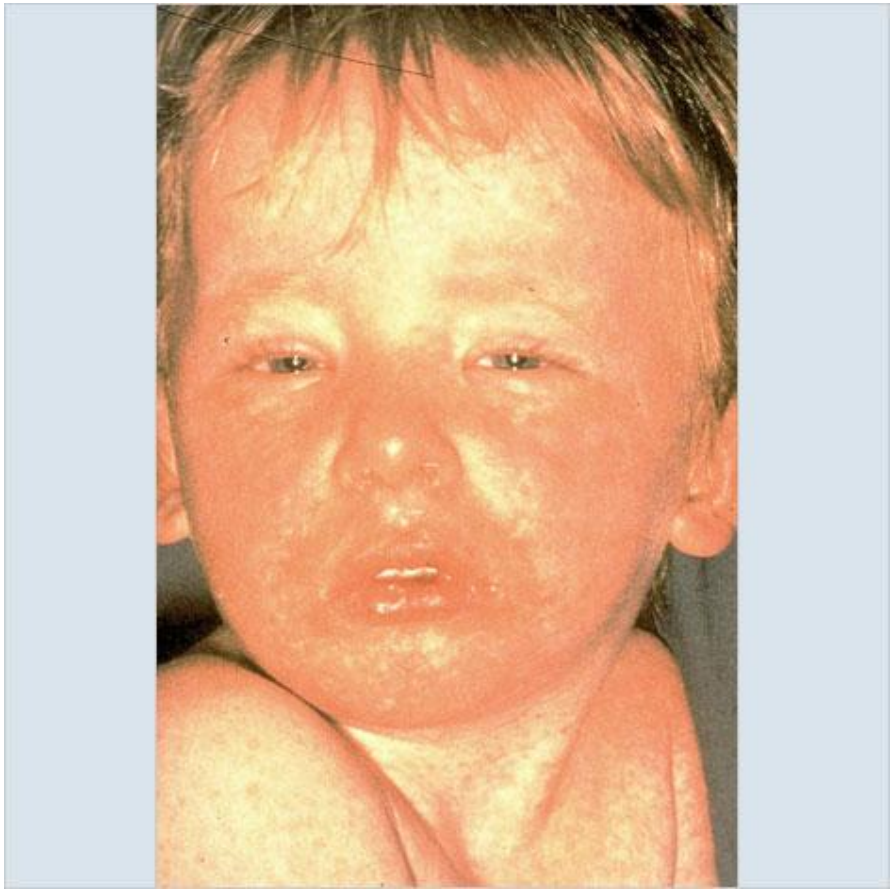
Fall Armyworm

www.ars.usda.gov

Influenza Vaccines
if Person Has a History of Egg Allergy

Trade Name	Abbreviations	Reaction to Eggs	
		Mild to Moderate	Severe
	Can Receive Influenza Vaccine?		
FluMist	LAIV4	No	No
Flublok	RIV3	Yes	**Yes**
Flucelvax	ccIIV3	Yes but watch 30”	No
All other influenza vaccines	IIV3 & IIV4	Yes but watch 30”	No

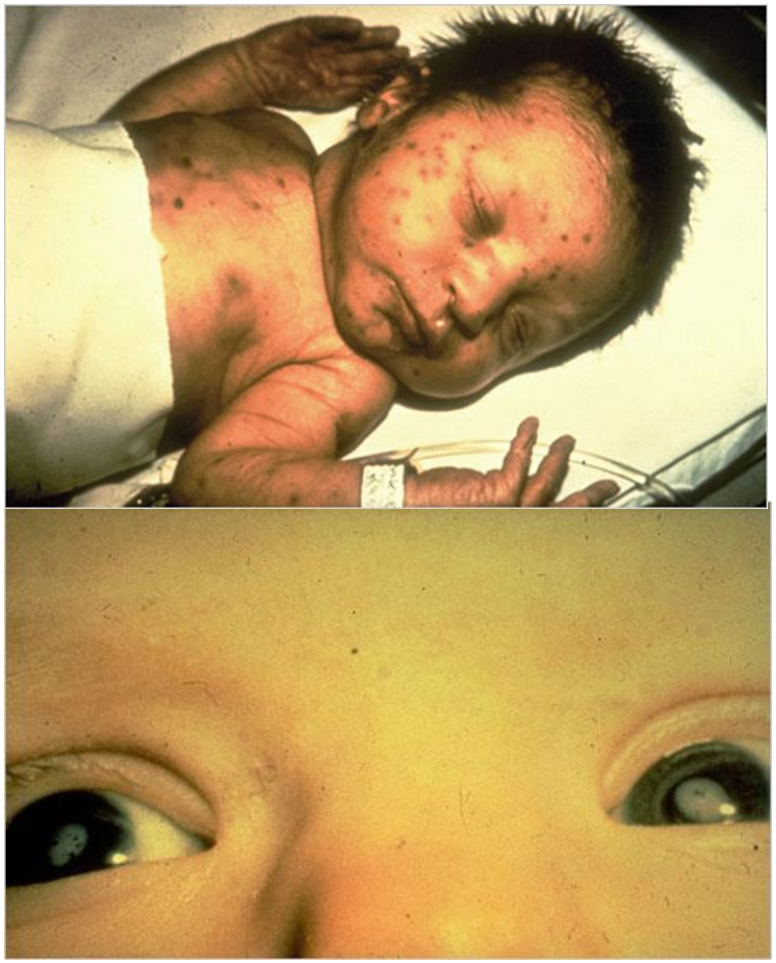
Complications of Measles



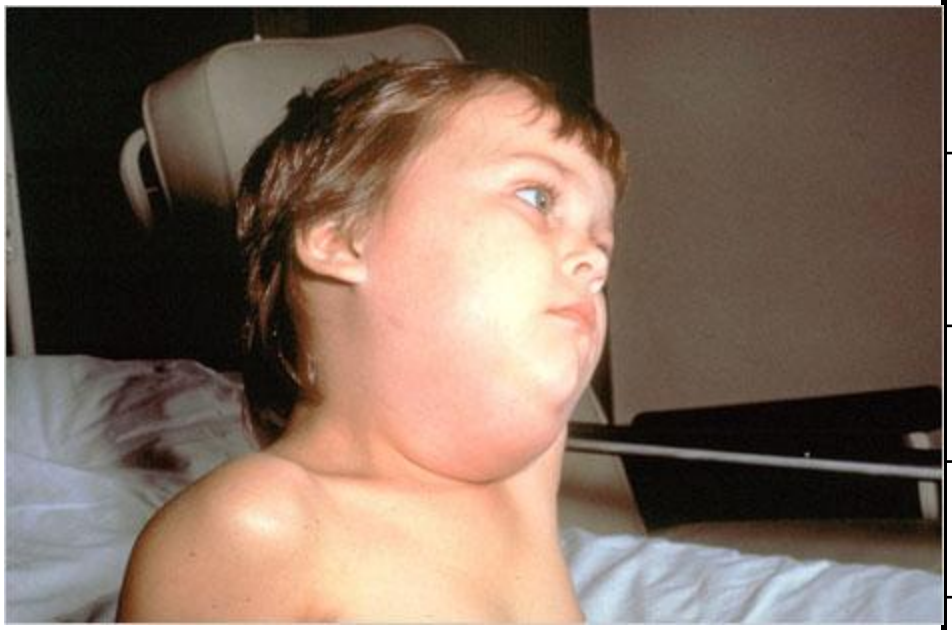
Measles in US 1985-1992	
%	Complications
8	Diarrhea
7	Otitis media
6	Pneumonia
0.6-0.7	Seizures
0.1	Encephalitis
0.2	Death

Congenital Rubella Complications

- Deafness
- Cataracts
- Retinitis
- Heart defects
- Microcephaly
- Mental retardation
- Skin rash



Complications from Mumps



Illness	Frequency
CNS disease	15% clinical cases
Orchitis	20-50% post pubertal males
Pancreatitis	2-5%
Deafness	1/20,000
Death	~1/year (1980-1999)

Children and MMR

- Two doses
  - 1st dose ≥ 12 months
  - 2nd dose 4-6 years
- Minimum time between dose 1 & 2
  - Four weeks
- Lower age decreases to 6 months
  - International travel
  - Exposure to measles (within 72 hours)

Adults & Measles Vaccine

- Born before 1957—presumed immune
  - Health care providers should get 2 MMRs
- Born ≥ 1957: 1 dose MMR
  - 2nd dose for HCPs, international travel, attending postsecondary educational institution

- Provider diagnosis of measles, mumps, or rubella is not acceptable

Measles Postexposure Prophylaxis for Nonimmune

- MMR within 72 hours of exposure
  - Ages ≥ 6 months and immunocompetent
- Immune globulin within 6 days of exposure
  - Infants (0-11 months)
    - IGIM 0.5 mL/kg (max 15 mL) both immune competent and immune compromised
  - Pregnant and severely immune compromised
    - IGIV 400 mg/kg

Immunity to Rubella and Mumps

Rubella

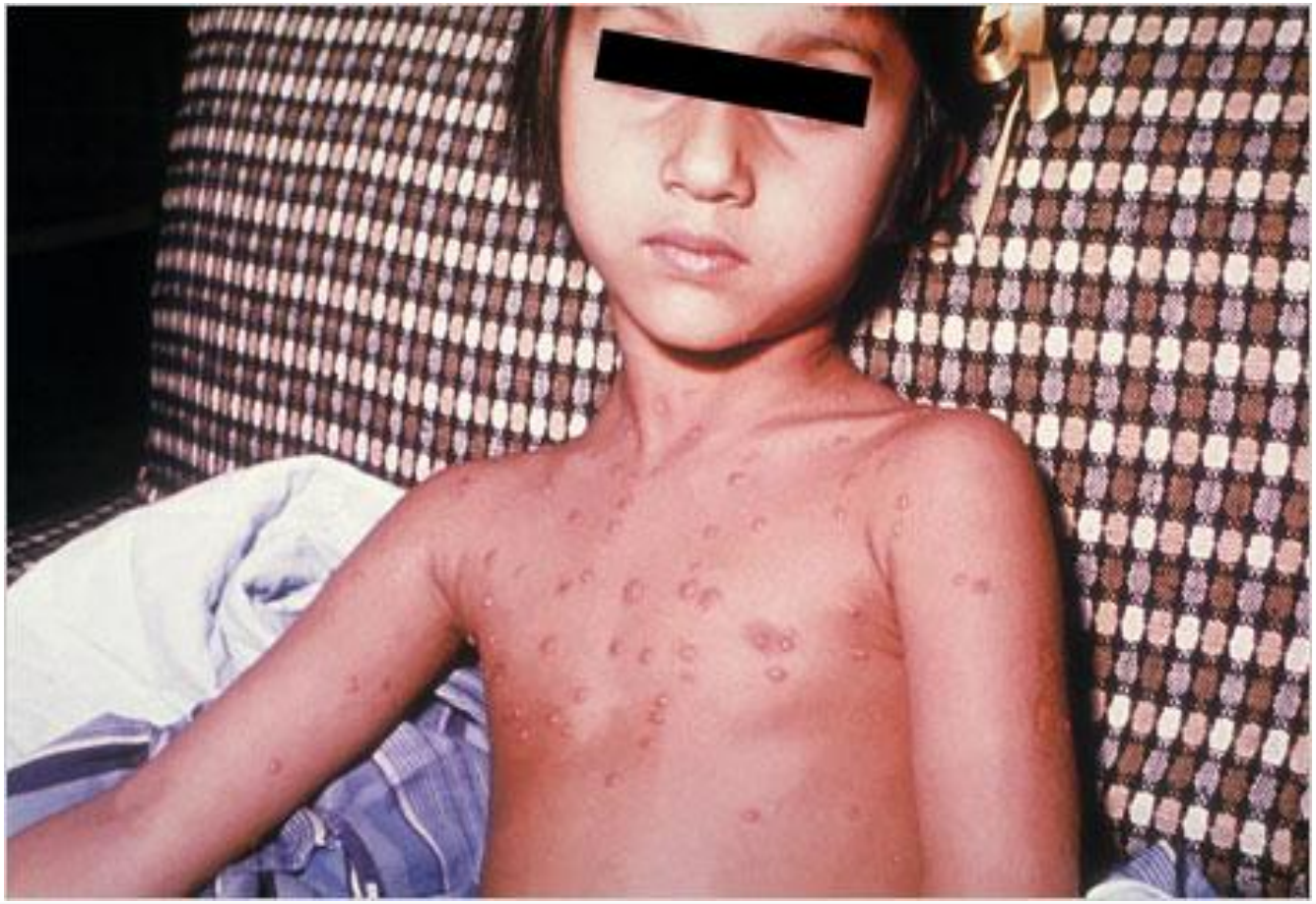
- Born before 1957 unless female of childbearing age
- Single dose of rubella vaccine
  - 3 maximum doses
- Positive serology
- Laboratory confirmation of disease

➢ Health care provider rubella diagnosis is not valid

Mumps

- Born before 1957
- Positive serology
- Laboratory confirmation of disease
- One dose MMR
  - Preschool or low risk adult
- Two doses of MMR for
  - International travel
  - Health care provider
  - Student in postsecondary educational institution

Varicella



Immunity to Varicella

- Two documented varicella vaccines
- Laboratory evidence of antibodies or disease
- History of zoster based on health-care provider's diagnosis
- Verification of typical disease by health-care provider
- Born in US before 1980
  - Exemptions: pregnancy, immune suppressed, HCP

Varicella Vaccine

- 2 doses
  - Minimum intervals
    - ≥ 13 years: 1 month
    - 1 year-12 years: 3 months

- If pregnant woman with varicella 5 days before-2 days after delivery, infant must receive VariZIG

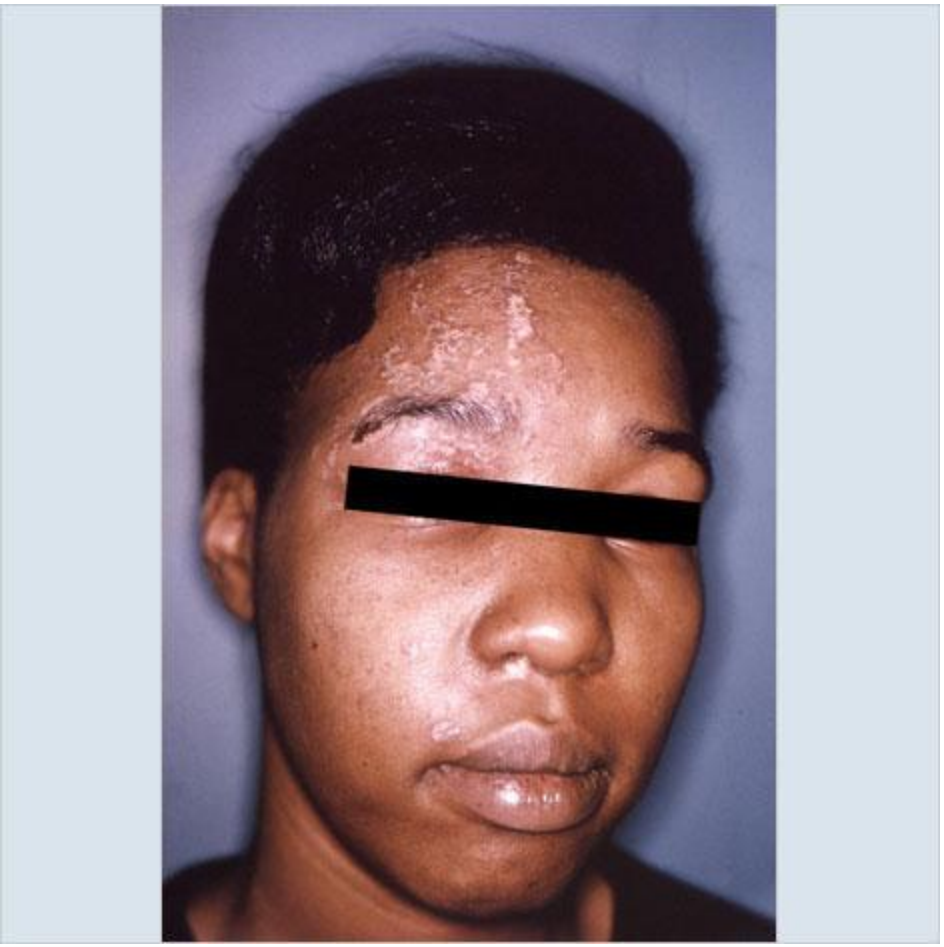
Interactions of Live Vaccines

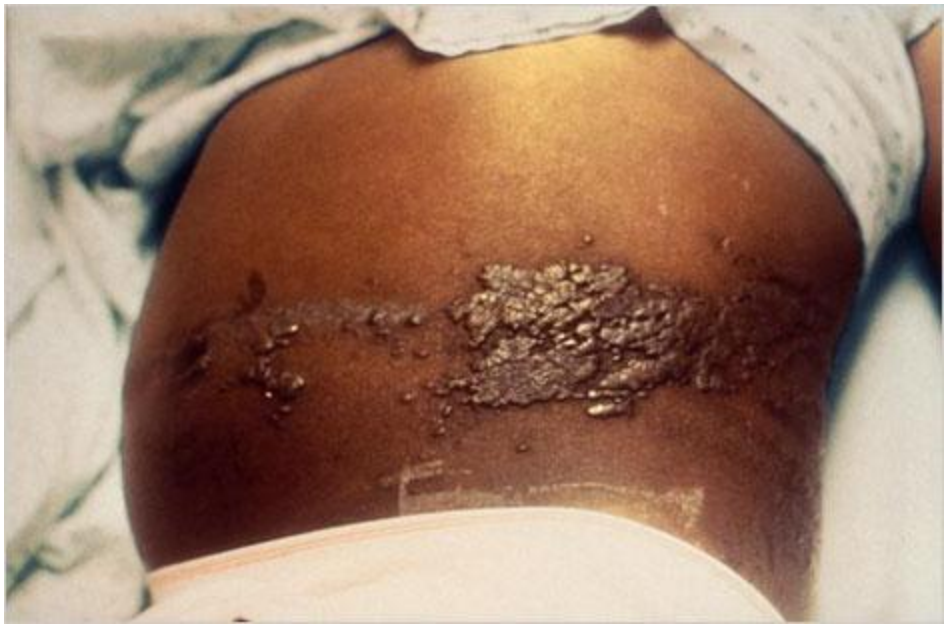
- Give on same day or 4 weeks apart
  - MMR, Varicella, LAIV

- Oral live vaccines do not have to have spacing intervals from other live vaccines
  - Rotavirus
  - Oral typhoid
  - Oral polio

CDC. Pink Book. 12th edition.

Shingles
(Reactivation of Varicella Zoster Virus)

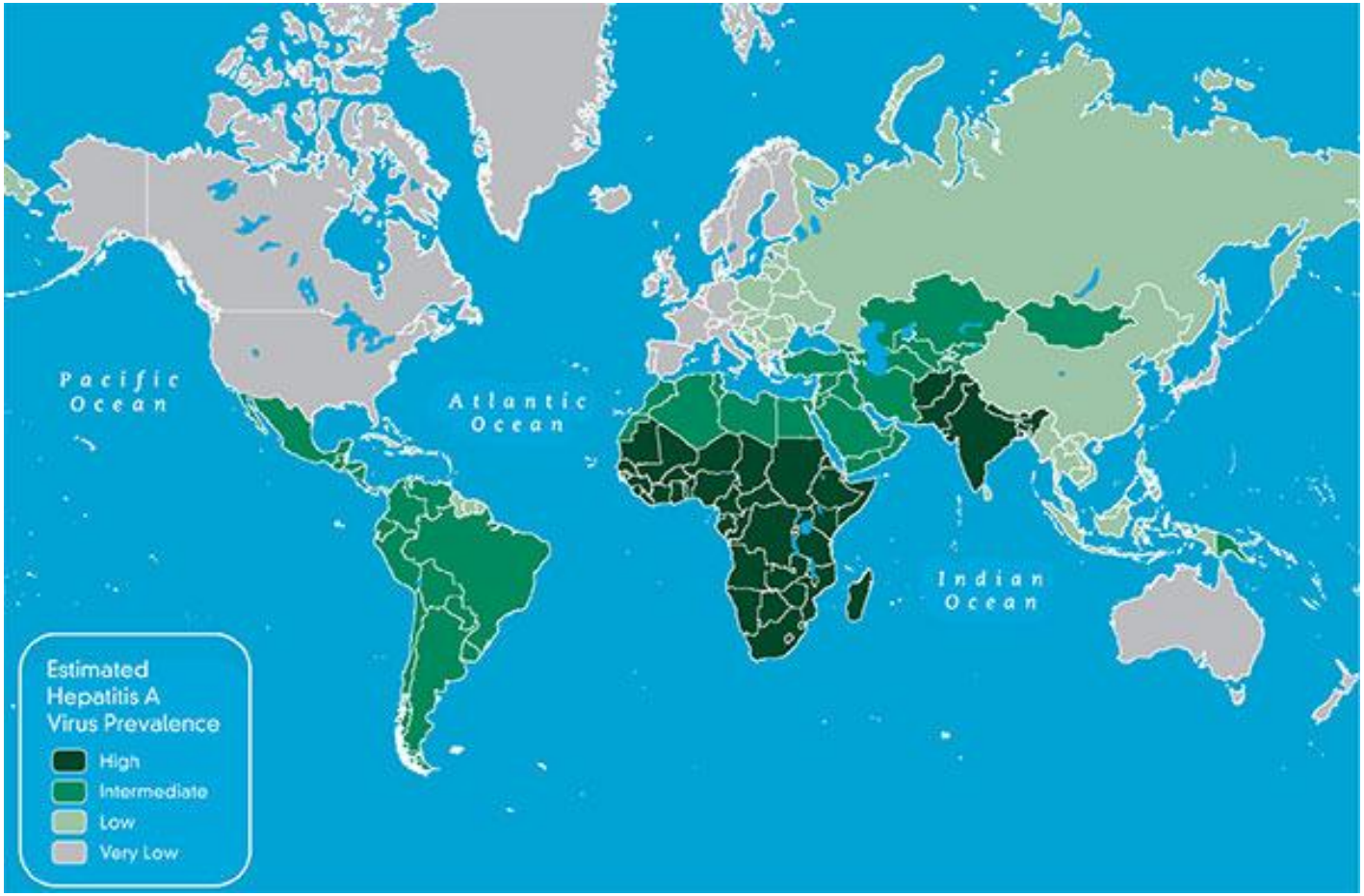




Zoster Vaccine

- 14 times the varicella virus as chicken pox vaccine
- No need to check varicella antibody status before giving
- Contraindicated in immunodeficiency, pregnancy, anaphylaxis to: gelatin, neomycin, zoster vaccine
- FDA licensed ≥ **50** years old
  - ACIP recommends ≥ **60** years old

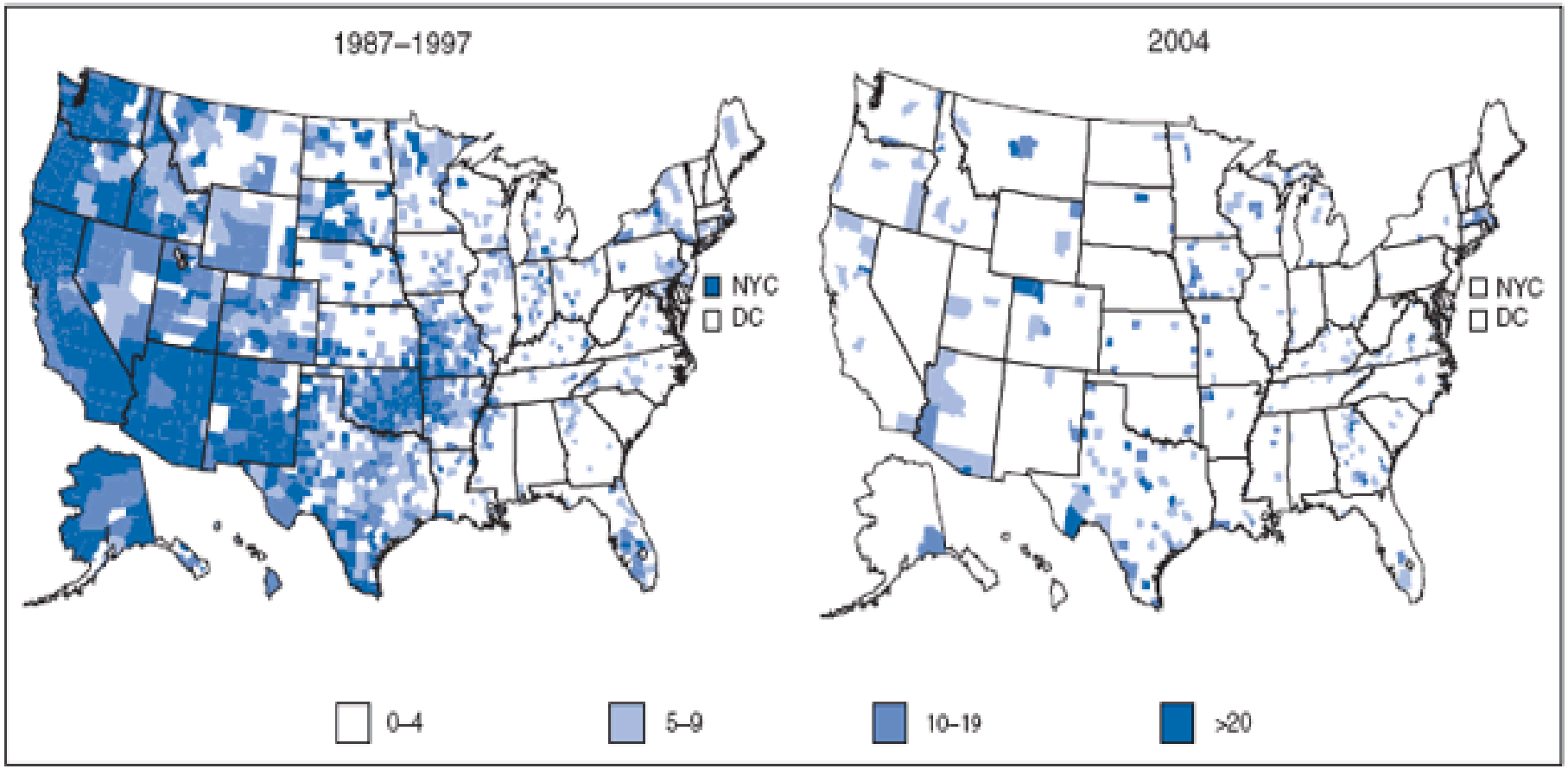
Hepatitis A Prevalence



www.cdc.gov

Decline in Hepatitis A with Vaccination

FIGURE 3. Rate* of hepatitis A, by county — United States, 1987–1997 and 2004



SOURCE: National Notifiable Diseases Surveillance System.
* Per 100,000 population.

MMWR May 19, 2006

Hepatitis A Vaccination

- Children 12-23 months
  - Routine
  - 2 dose
  - 2nd dose 6-18 months after 1st
- Give to older children if protection desired
- Give to the high risk

High Risk for Hepatitis A

- Travel or work where intermediate or high
- Close contact with international adoptee within 60 days of arrival from higher risk area
- Injection and non-injection illicit drug use
- Clotting-factor disorders
- Chronic liver disease
- MSM
- Work with Hepatitis A infected primates/lab

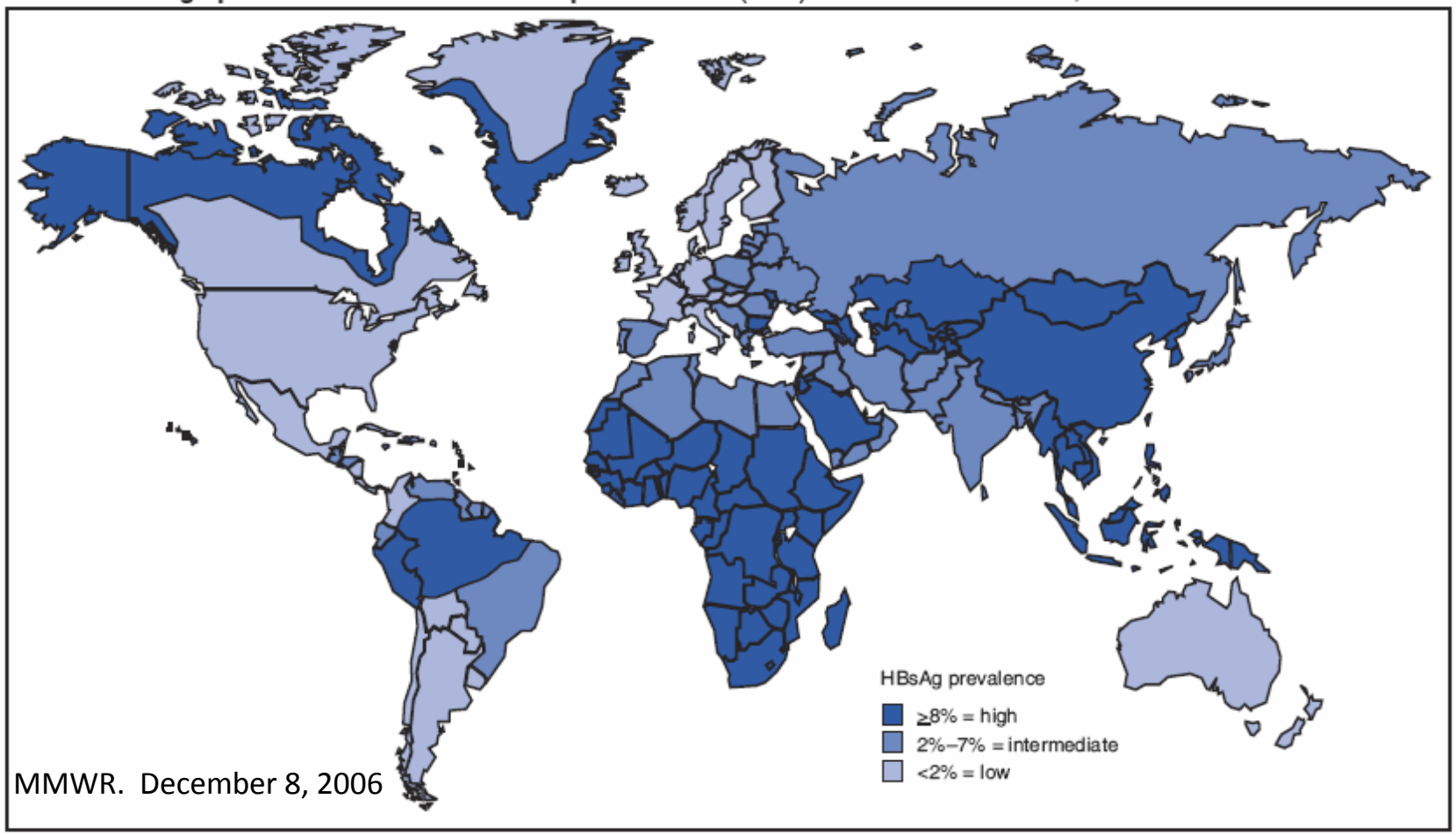
Hepatitis A Vaccines

- Havrix or Vaqta: 0, 6-18 months
  - Peds and adult formulations
- Twinrix (A & B): Ages ≥ 18 years
  - 0, 1, 6 months
  - 0, 7 days, 21-30 days, 12 months

- Havrix or Vaqta can be used as postexposure prophylaxis within 2 weeks for ages 1 yr-40 yo
- Use IGIM (0.02 mL/kg) for < 1 yo, > 40 yo, underlying medical conditions

Chronic Hepatitis B Infection, 2005

FIGURE 4. Geographic distribution of chronic hepatitis B virus (HBV) infection — worldwide, 2005*



MMWR. December 8, 2006

Risk Factors for Hepatitis B

- > 1 sex partner in 6 mos
- STD evaluation or Rx
- MSM
- HIV infected
- Injection drug users
- Correctional facilities
- Facilities for care of developmental disabilities
- Health care personnel
- Public safety workers
- Diabetics < 60 yo
- Chronic hemodialysis
- End stage renal disease
- Chronic liver disease
- Travelers to countries with high or mod HepB

Hepatitis B Formulations

- Monovalent
  - Recombivax & Engerix B
- Pediatric/Adol & Adult & Dialysis
- Twinrix (A & B)
- Combination (peds)
  - Comvax (Hib-HepB)
  - Pentacel (DTaP-IPV-HepB)

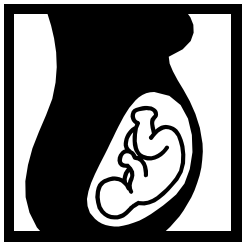
- Standard dosing
  - 0, 1-2, 6 months
- Alternate dosing
  - 0, 1-2 mo, 4 mo
- Infancy: Min age for 3rd dose
  - 24 weeks
- Twinrix (A & B)
  - 0, 1 mo, 6 mo
  - 0, 7d, 21-30 d, 12 mo
- 11-15 yo using Merck adult formulation: 0, 4-6 mo

Preventing Perinatal Hepatitis B

Mother's HBsAg at Birth	Infant	Needed Actions	Other
Positive	Any weight	HBIG and HBV vaccine within 12 hours of birth	Finish vaccine series ASAP, then check HBsAg and anti-HBsAf
Negative	Any weight	HBV vaccine before discharge	Finish series
Unknown	< 2 kg	HBIG and HBV vaccine within 12 hours of birth	Check mother's HBsAg ASAP. Don't count 1st dose Finish series
Unknown	≥ 2 kg	HBV within 12 hours of birth	Check mother's HBsAg ASAP
		If mom HBsAg positive, give HBIG ASAP, up to 7 days	Finish series ASAP

Serology after Hepatitis B Vaccine Needed if…

- Infant born to hepatitis B infected mother
- Health care provider
- Hemodialysis patient
- HIV infected
- Immune compromised
- Sex partner of person chronically infected with hepatitis B



Vaccines and Pregnancy

Contraindicated

- Live, attenuated
  - MMR
  - Varicella
  - Zoster
  - LAIV
  - Oral typhoid
- Inactivated
  - HPV

Give if Needed

- **Influenza**
- **Tdap**
- PCV13
- PPSV23
- Hib
- MCV4
- IPV
- Hepatitis A or B

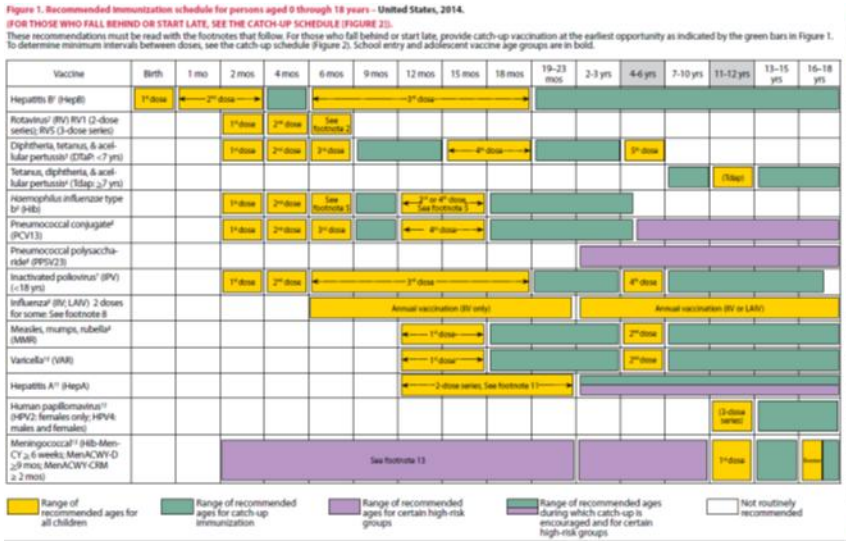
Contraindications to Vaccines

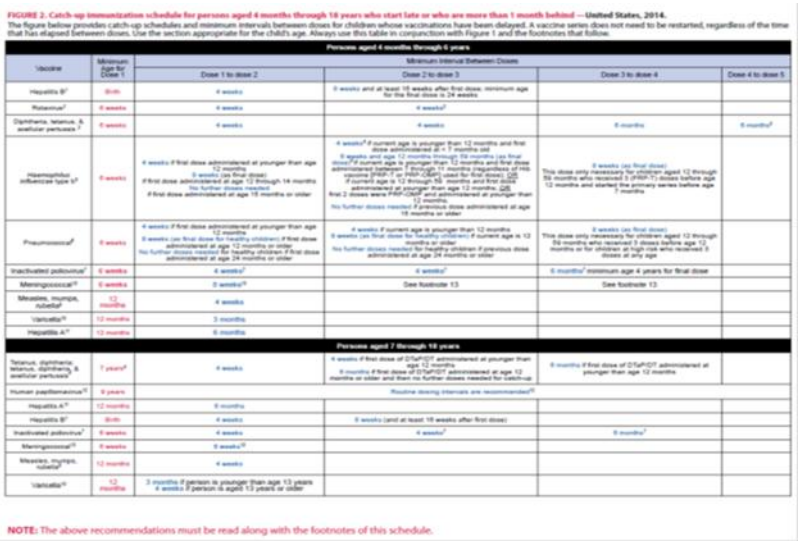
- Anaphylaxis to previous dose or vaccine component
- Moderate to severe illness
- Live vaccines: Immune compromise or pregnancy
- Child who developed encephalopathy without another explanation within 7 days of pertussis-containing vaccine

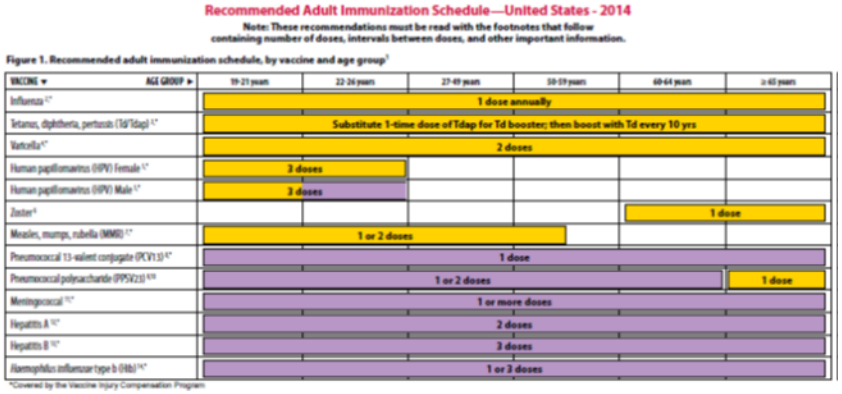
Precautions

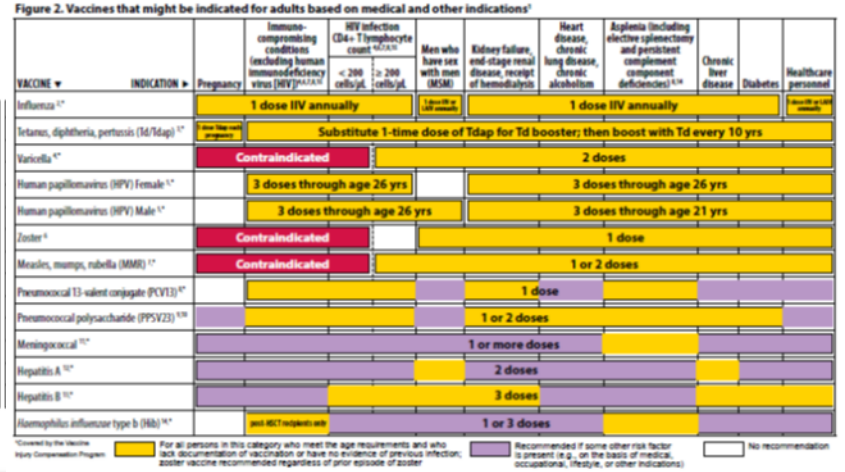
- MMR or VZ and recent immune globulin or antibody-containing blood product
- Guillain-Barré Syndrome within 6 weeks of influenza or tetanus-containing vaccine
- Mild reaction to eggs (influenza vaccines)
- Antiviral therapy (influenza & varicella)
- Unstable neurologic status (pertussis)
- History of thrombocytopenia (MMR)
- Need to do TB skin test (MMR)

Questions?









http://www.cdc.gov/vaccines/schedules/index.html